

Prognostic factors in patients with intracerebral haematoma

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Abstract

In a prospective study, the prognostic value of clinical characteristics in 157 consecutive patients with spontaneous supratentorial intracerebral haemorrhage were examined by means of multivariate analysis.

Two days after the event 37 (24%) patients had died. Factors independently contributing to the prediction of two day mortality were pineal gland displacement on CT of 3 mm or more ($p < 0.001$), blood glucose level on admission of 8.0 mmol/l or more ($p = 0.01$), eye and motor score on the Glasgow Coma Scale of eight out of 10 or less ($p = 0.022$) and haematoma volume of 40 cm³ or more ($p = 0.037$). Between the third day and one year after the event another 46 of the 120 two day survivors had died; the independent prognostic indicators for death during that period were: age 70 years or more ($p < 0.001$) and severe handicap (Rankin grade five) on the third day ($p < 0.001$). Functional independence (Rankin grade two or less) at one year was most common not only with the converse features of age less than 70 years ($p < 0.01$) and Rankin grade four or less on the third day ($p = 0.002$), but also with an eye and motor score on the Glasgow Coma Scale of nine or 10 on the third day ($p < 0.001$).

The 120 patients with intracerebral haemorrhage who were still alive two days after the event were matched with 120 patients with cerebral infarction, according to age, level of consciousness on the third day after stroke (Glasgow Coma Scale) and handicap (Rankin grade). Survival and handicap after one year did not differ between these two groups. The conclusion drawn is that it is not the cause (intracerebral haemorrhage or cerebral infarction) but the extent of the brain lesion that determines the outcome in patients who survive the first two days.

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It is well known that patients with intracerebral haematoma (ICH) have a high death rate, especially in the first few days.¹⁻⁵ Factors such as the score on the Glasgow Coma Scale (GCS), the size of the haematoma, age, rupture of the haemorrhage in the ventricular system, midline shift and pulse pressure have been identified as determinants of outcome

in multivariate analysis.⁶⁻⁹ In contrast, the mortality from cerebral infarction (CI) is lower and usually occurs later than the first two days after stroke.¹⁻¹⁰ Studies that compared outcome after ICH with that after CI generally mention a better prognosis for patients with CI.^{1-5, 11-14} Only one study found no significant difference in outcome after one year.¹⁵ All these studies compared consecutive groups of patients with ICH or CI, independent of age, level of consciousness or disability on admission.

In this prospective study, we analysed the short term (two days) and the long term prognosis of patients with supratentorial ICH, and we also compared those patients with ICH who survived the first two days with a matched group of patients with CI.

Patients and methods

We prospectively studied 157 consecutive patients with spontaneous supratentorial ICH who were admitted to the De Wever-Ziekenhuis in Heerlen ($n = 96$) and the University Hospital in Utrecht ($n = 61$), from October 1986 to September 1989. Their ages ranged from 33 to 91 years (mean 68 years); 89 patients were men (57%). Patients where aneurysmal bleeding was suspected from the site of the haematoma were excluded. Ninety-six per cent of the patients were admitted to hospital within 24 hours after the haemorrhage and 75% within three hours. The eye and motor score on the GCS was used as a measure of the level of consciousness; the verbal score was not taken into account because many patients were unable to speak due to aphasia or because they were intubated. With this modification, the maximum on the GCS is 10. The modified Rankin scale is a useful measure of handicap, particularly in the long term.^{16, 17} For the assessment of outcome after one year, the Rankin scale was contracted into two categories: functionally independent (corresponding to grades zero, one or two) and functionally dependent (corresponding to grades three, four or five). The severity of the hemiparesis was estimated according to the Medical Research Council scale, in the most severely affected muscle groups and dichotomised in severe (0-2) versus moderate to no hemiparesis or normal power (3-5). Blood glucose levels could be obtained in all but 19 patients. Motor power in deeply unconscious patients ($n = 3$) who could not respond to command or react on a painful stimulus was graded as severe hemiparesis.

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The diagnosis of ICH was confirmed by CT in 156 patients and by post mortem examination in one patient. The haematoma volumes were measured from the first CT scan, directly from the video screen or by means of the best fit method.¹⁸ Two neurologists assessed the CT scans according to site and volume of the haematoma, rupture into the ventricular system and midline shift. None of the patients was surgically treated.

The 120 patients who were still alive two days after ICH were matched with 120 patients with supratentorial CI. These patients had been admitted to the same hospitals and during the same period as the patients with ICH. Eighty nine per cent of the patients with CI had been admitted to hospital within 24 hours after stroke (54% within three hours). All patients with CI were investigated by CT. The patients were primarily matched according to Rankin grades, and as near as possible according to age (approximately 10 years) and according to the eye and motor score of the GCS (approximately 2) on the third day after stroke.

The sum of the GCS eye and motor score on the third day after stroke differed slightly between the two patient groups: 34 patients with ICH had a score of eight or less versus 23 CI patients. The frequency of definite stroke in the past, the use of oral anticoagulants or a history of peripheral vascular disease were similar in the two groups. Diabetes mellitus, a history of atrial fibrillation or a history of other heart disease were more frequent in the patients with CI. A systolic blood pressure on admission of more than 160 mm Hg was found in 67% of the patients with ICH, against 42% of the patients with CI, but a diastolic blood pressure of more than 90 mm Hg was almost equally common in both groups (59% of the patients with ICH and 49% in patients with CI). The severity of the hemiparesis was similar in the two patient groups. The mean blood glucose level and the percentages of patients with serum glucose values of 8 mmol/l or more on admission did not differ between the two patient groups.

All surviving patients with ICH or CI had a

neurologic evaluation at three, 14 and 30 days, and at four, eight and 12 months. In the univariate analysis, the proportion of deaths or a good outcome in patients with a certain characteristic (for instance severe hemiparesis) was compared with that in patients without the characteristic employing relative risk. The 95% confidence interval was used to describe the precision of the relative risk. Variables selected from univariate analysis were sequentially entered into a logistic model until no remaining candidate variable met a significance level of $p = 0.05$. The odds ratio (OR) resulting from the logistic model may be interpreted as relative risks. If a patient has more than one of the characteristics selected in the model, the risk of death relative to that in a patient without those characteristics is obtained by multiplying the odds ratios of those characteristics. The χ^2 test was used where appropriate.

Results

Baseline characteristics of the patients with ICH are presented in table 1. The ICH occurred on the right side in 78 and on the left side in 79 patients. A lobar haematoma occurred in 60 patients and a haematoma in the basal ganglia in 97 patients. No significant difference in age, haematoma volume, history of hypertension, or use of oral anticoagulants existed between patients with a lobar or basal ganglia haematoma. Headache on admission was significantly more common in patients with lobar haematoma (52%) than in patients with basal ganglia haematoma (28%) ($p < 0.01$). Early seizures occurred in 13 (8%) patients, in nine (15%) with a lobar haematoma versus four (4%) with a basal ganglia haematoma ($p < 0.05$). Vomiting on admission ($n = 63$) occurred equally in both groups. Rupture of the haematoma in the ventricular system occurred significantly more often in patients with a basal ganglia haematoma (54%) than in lobar haematomas (35%) ($p < 0.05$). In patients with lobar haematomas the fourth ventricle was never completely filled with blood. The 27 patients who were on oral anticoagulants at the time of the event had a

Table 1 The occurrence of two day and third day to one year mortality in relation to several clinical characteristics at the time of the bleeding in 157 patients with intracerebral haemorrhage

Variable (n)	Two day mortality				Third day to one year mortality				
	n	%	RR	(95%CI)	Total (n)	n	%	RR	(95%CI)
All patients (157)	37	24	—	—	(120)	46	38	—	—
Age ≥ 70 years (83)	22	27	1.3	(0.7 to 2.3)	(61)	35	57	3.1	(1.7 to 5.5)
History of hypertension (59)	13	35	0.9	(0.5 to 1.6)	(46)	15	33	0.8	(0.5 to 1.3)
Eye and motor score (GCS) \leq eight (50) on the first day	25	50	4.5	(2.4 to 8.1)					
Eye and motor score (GCS) \leq eight on the third day					(34)	29	85	4.3	(2.7 to 6.7)
Vomiting (63)	16	25	1.1	(0.6 to 2.0)	(47)	24	51	1.7	(1.1 to 2.6)
Plantar reflexes with a left and right extensor response (23)	15	65	3.4	(2.4 to 6.4)	(8)	5	62	1.7	(0.9 to 3.1)
Severe hemiparesis (104)	35	34	8.9	(2.2 to 35.7)	(69)	36	52	2.7	(1.5 to 4.8)
Blood sugar ≥ 8 mmol/l or missing (79)	32	40	6.3	(2.6 to 15.4)	(47)	27	57	2.1	(1.4 to 3.5)
Basal ganglia or thalamic haematoma (97)	27	28	1.7	(0.9 to 3.2)	(70)	26	37	0.9	(0.6 to 1.5)
Haematoma volume ≥ 40 cm ³ (61)	31	51	8.1	(3.6 to 18.3)	(30)	23	77	3.0	(2.0 to 4.5)
Haematoma rupture into the ventricular system (73)	32	44	7.4	(3.0 to 17.9)	(41)	25	61	2.3	(1.5 to 3.6)
Fourth ventricle dilatation and filled with blood (14)	7	50	2.4	(1.3 to 4.4)	(7)	5	71	1.3	(0.8 to 2.1)
Lateral ventricular dilatation (40)	22	55	4.3	(3.5 to 7.4)	(18)	13	72	2.2	(1.5 to 3.3)
Lateral ventricular compression (89)	26	29	1.8	(1.0 to 3.4)	(63)	28	44	1.4	(0.9 to 2.3)
Pineal gland displacement ≥ 3 mm (51)	32	63	13.3	(5.5 to 32.1)	(19)	14	74	2.3	(1.6 to 3.4)
Rankin grade five on the first day (122)	37	30	—	—					
Rankin grade five on the third day	—	—	—	—	(77)	42	55	5.9	(2.3 to 15.2)

RR = relative risk; CI = confidence interval

mean haematoma volume of 51 cm³, versus 33 cm³ in patients with ICH not receiving anticoagulants ($p = 0.058$).

Death from transtentorial herniation within two days occurred in 37 (24%) of the 157 patients with ICH, 32 of whom died within one day. The mean age of these 37 patients was 70 years (range 48–89). A history of hypertension or the use of oral anticoagulants was equally common in these 37 patients as in the 120 patients with ICH who survived the first two days. All 37 patients who died early had been completely dependent (Rankin grade five) on admission. The GCS (where the maximum is 10) the score was nine or 10 in 12 patients who died early and eight or less in the remaining 25 patients. Fifteen of the 19 patients (79%) in whom the blood glucose level was not determined died within two days. In a multivariate analysis, the risk of death within two days was determined by displacement of the pineal gland of 3 mm or more (OR = 14, $p < 0.001$), blood glucose level on admission of 8 mmol/l or more (including patients with missing values) (OR = 5.5, $p = 0.01$), eye and motor score of eight or less on the GCS (OR = 3.9, $p = 0.022$) and haematoma volume of 40 cm³ or more (OR = 3.6, $p = 0.037$). In the subgroup of patients with Rankin grade five on admission ($n = 122$), the two day mortality was determined by the same characteristics. Exclusion of the 19 patients with a blood glucose level which was not determined yielded essentially the same model. The 30 day case fatality rate in all patients with ICH was 43% (68 of the 157 patients).

After 12 months, 83 of the 157 patients (53%) with ICH had died. The death rate at one year did not differ between patients with or without anticoagulants (15 of 27 [56%] and 68 of 130 [52%], respectively). The one year mortality in the two groups with lobar or basal ganglia haematoma was also similar, 50% and

Table 2 Main causes of death in the 120 patients with intracerebral haemorrhage who survived the first two days and their matched controls with cerebral infarction

Main cause of death	ICH	%	CI	%
Infection	16	34	19	41
Tentorial herniation	11	24	8	17
Ischaemic heart disease	5	11	7	15
Recurrent stroke	4	9	2	5
Pulmonary embolism	3	7	3	7
Miscellaneous	7	15	7	15
Total	46	100	46	100

ICH = intracerebral haemorrhage; CI = cerebral infarction

55%, respectively. The occurrence of early seizures did not influence outcome. In the multivariate analysis of the risk factors for death between the third day and one year after the event, the predictors were age of 70 years or more (OR = 6.1, $p < 0.001$) and severe handicap (Rankin grade five) on the third day (OR = 9.5, $p < 0.001$). Sex, history of hypertension, systolic and diastolic blood pressure, pulse pressure, the side of the stroke, changes in Rankin grade, and eye and motor scores between admission and the third day, did not independently contribute to the model, nor did the variables not mentioned above but listed in table 1. Functional independence at one year (43 patients) was determined by an age of less than 70 ($p < 0.001$), eye and motor score of nine or 10 on the GCS on the third day ($p < 0.001$), and Rankin grade four or less on the third day ($p = 0.002$).

The outcome after 12 months in the 120 patients with ICH who were still alive after two days did not differ from that in the 120 matched controls with CI. Forty six patients in both groups had died (fig). After adjustment for differences in baseline characteristics, the mortality in the two patient groups was also similar. Recurrent stroke occurred in four patients with ICH (all fatal) and in three patients with CI (two fatal). Sixteen patients (six with ICH and 10 with CI) died between the fifth and twelfth month; this number significantly exceeded the expected total number of deaths (five) in an age matched and sex matched group from the general population. Twelve months after the stroke, 43 patients with ICH and 41 patients with CI (both about one third of the original group) were functionally independent. The distribution of the Rankin grades was also the same at the different intervals within the 12 month follow up period (fig). The main causes of death after the second day were similarly distributed (table 2). Altogether 45% of the deaths between two days and one year were caused by complications of immobility, particularly infections and pulmonary embolism.

Urinary and faecal incontinence after two weeks was a prognostic indicator for survival at one year in patients with ICH as well as with CI: 41 of the 90 patients (46%) with incontinence had died at 12 months, versus 12 out of 105 (11%) without incontinence (relative risk 4.0, 95% confidence interval 2.2 to 7.1). For six patients no information about continence was available; none of them died.

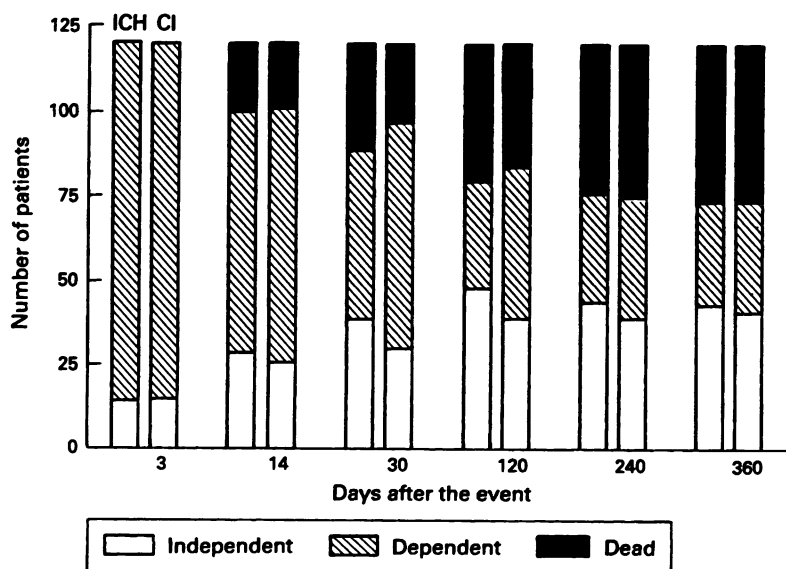


Figure The change in the contracted Rankin scale (functionally independent [Rankin grades zero to two] or dependent [Rankin grades three to five]) from the third day to one year in the 120 patients with intracerebral haemorrhage (ICH) (left bars) and cerebral infarction (CI) (right bars).

Discussion

The initial mortality after ICH is high and occurs mostly within one or two days. After that time, the chance of recovery in patients with ICH is similar to that in patients with ischaemic stroke. This means that once the danger of cerebral herniation has passed, it is the extent and not the cause of the structural brain damage that determines the prognosis.

The proportion of patients with ICH who died within the first two days (24%) corresponds with that reported in other studies.^{1 11} The independent indicators for early death in our study were: pineal gland displacement, a high blood glucose level on admission (8 mmol/l or more), the eye and motor score on the GCS, and the haematoma volume. Some previous studies with multivariate analysis in patients with ICH found other indicators for prognosis, but these determined outcome on discharge,⁴ at 30^{6 9 11} or 60 days,⁷ or at six months⁸ after the haemorrhage. The variables selected in those cases were rupture of the haematoma in the ventricular system,⁹ hypertension and pulse pressure.⁷ The level of consciousness^{4 6 7 8 11} and haematoma volume or size,^{4 6 8 9} have also been identified as prognostic indicators, as in our study. The importance of pineal gland displacement confirms that the space the haematoma occupies is an important determinant of early outcome. A relation between pineal gland displacement and impairment of consciousness has been identified in previous studies,^{19 20} but we found these two factors independently predicted mortality within two days. Hyperglycaemia on admission as an indicator of a poor prognosis in patients with ICH has been reported before.²¹ The hyperglycaemia is probably not directly harmful to the brain but reflects stress relating to stroke severity.²¹ The strong relationship with early death is only partly explained by inclusion of the 19 patients in whom no glucose level was available, usually because their clinical condition was judged too poor to justify the collection of a blood sample.

The death rate of 53% one year after the event in patients with ICH is much higher than that in another study (34%),²² but only 32% of the patients in that study were admitted to hospital within 24 hours, against 96% in ours. The very short delay between ICH onset and hospital admission in our study, meant that even moribund patients still reached the hospital alive. It is possible, but not likely, that milder cases with ICH have not been referred, as the 30 day mortality in our study (43%) was only slightly higher than that in a recent population based study from Italy (38%),¹⁴ and lower than that in the Oxfordshire community study (52%).⁵ We found severe handicap (Rankin grade five) on the third day and not the level of consciousness as prognostic indicator for mortality at one year; of the 77 patients with severe handicap on day three, 38 had a normal level of consciousness. Twenty seven per cent of all patients (n = 43) with ICH reached functional independence at one year, which is in accordance with a previous

and prospective community study.⁵ Age and level of consciousness as prognostic indicator of good clinical outcome 12 months after ICH in our study confirmed the finding in a former study without multivariate analysis.²² One study with multivariate analysis found as independent predictors of satisfactory outcome at six months: age, haemorrhage size, rupture of the haematoma in the ventricular system, limb weakness and communication disorders.⁹ Our results also confirm previous studies about incontinence in patients two weeks after stroke as a predictive factor for one year mortality.^{23 24}

The patients with ICH who survived the first two days had a similar outcome as patients with CI who were matched according to Rankin grade, age and level of consciousness. This similarity applies to the proportion of dependent patients during follow up as well as to the number of patients who died and the causes of death. Previous studies found differences in 30 day mortality rates in favour of patients with ICH from 28 to 46% (30 day mortality rate of 38 to 66% in patients with ICH versus 10 to 20% in patients with CI).^{1 5 11 12 14} Between the thirtieth day and one year, roughly the same mortality rate (10–16%) has been reported for patients with ICH or CI.^{1 5 11 12} In only two studies,^{5 14} CT confirmation was never¹² or only rarely^{1 11} available. After the high initial death rate in patients with ICH in the first weeks, these studies found no differences in late mortality rate between non-matched groups of patients with ICH or CI.^{5 11 12 14} A previous prospective population study with multivariate analysis also identified age and severity of stroke (minor stroke versus major stroke) as prognostic indicators for survival one year after the event, and not the subtype of stroke (ICH or CI).¹⁵ The same study did not find an excess in mortality between five and 12 months compared with the general population,¹⁵ in contrast to our study. The excess mortality in our study is probably the result of our method of matching, by which we have purposely excluded milder cases of ischaemic stroke.

We have insufficient reason to suppose that the omission of surgical evacuation in our patients with ICH negatively influenced their outcome, as the benefits of this mode of treatment are not established.^{25–27} In a few patients, or operation was considered because of progressive deterioration before the stage of irreversible brain stem dysfunction, but they improved spontaneously. More trials of surgical treatment are necessary; the prognostic factors we found in this study may help in identifying those patients who could gain most from treatment.

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